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## **Response: Muscle Strength and Function Rather Than Muscle Mass in Sarcopenia**

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Dear Editor,

The authors welcome the constructive comments from Kara et al. concerning our recent paper (Lees et al. 2019). Their primary observations relate to the absence of gender from our analyses, the clinical relevance of our regression models, and use of non-specific muscle quality (MQ) cut-points. In the first instance, it is imperative to point out that we do not disagree in principle with any of the points raised, however we believe that we have either addressed or alluded to the related issues within the main manuscript.

The purpose of this pilot study was to highlight the importance of MQ as a conjunctive measure alongside established sarcopenia definitions. We agree with Kara et al. that reductions in muscle power and physical performance precede a decrease in muscle mass. This is why we included measures of upper and lower body strength alongside the assessment of muscle mass in our study design. Furthermore, we sought to investigate the utility of MQ given the recent emphasis of the European Working Group on Sarcopenia in Older People (Cruz-Jentoft et al. 2018). Our most notable finding was that 42% of the older group had low MQ at the upper body, and 50% at the lower body. This was in spite of only 2 – 4% of the older group being classified as sarcopenic using two established definitions. Hence, there is a clear need for methods to approximate and identify impaired MQ in older populations.

The absence of gender from our analyses was motivated by the unequal gender ratios between groups, and a desire to enhance statistical power. Two equations were calculated for the estimation of upper and lower body appendicular lean mass (ALM) in both groups. Maximum strength at the upper and lower body served as the strongest predictors of ALM in both groups, albeit to a greater extent in the younger group. We acknowledge that gender differences exist based on previous research (Musselman and Brouwer 2005), and in the third

paragraph of our introduction we state that age-related declines in lower body strength are of greater magnitude than those for upper body strength. Therefore, as we alluded to in our discussion, future studies should look to expand on our pilot work by assessing the efficacy of the regression models in more diverse and larger sample populations, where the role of gender in age-associated decrements in muscle mass and function might be further explored. When considering that most of the variance in strength is explained by muscle mass in both men and women (Newman et al. 2003), we believe that there is merit in cautiously applying our equations until gender- and population-specific variants are established.

The combination of upper and lower body strength measures enabled us to predict upper and lower body ALM to the strongest degree. Our rationale for using the regression models is to estimate upper and lower body ALM, which may then be cautiously implemented in the calculation of MQ. In a clinical setting, imaging equipment may not be readily available to measure muscle mass. By using the regression models, MQ can be estimated and then the patient referred for imaging if low MQ is suspected. In doing so, unnecessary exposure to ionising radiation may be minimised (Malone et al. 2012). We agree with Kara et al. that the decline in knee extensor strength with age occurs much earlier than that of handgrip strength. Whilst this is evidentially the case, neither of these variables are measured routinely in clinical practice, and schemes that have attempted to do so have focused exclusively on handgrip strength (Ibrahim et al. 2018).

The low mean age of our younger group is explained by the fact that all participants were recruited from the university and wider community in a random fashion. Regarding the point about the similar upper body MQ between groups, we provided a full explanation in paragraph five of the discussion where we also recognised the need for establishing age-specific MQ cut-points. In the methods, we also emphasised the absence of cut-points in

younger populations and clearly specified that the limited comparisons made with cut-points for older people should be treated with a degree of caution.

In summary, greater emphasis on lower body strength assessments alongside MQ estimation may improve surveillance of physical performance decrements in older people and mitigate the risk of poor healthcare outcomes. Future studies should look to investigate predictors of upper and lower body ALM using larger and more diverse sample populations.

Yours sincerely,

Matthew Lees, Dr Oliver Wilson, Dr Karen Hind, and Dr Theocharis Ispoglou

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**Conflict of Interest:** The authors declare that they have no conflict of interest.

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